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Authors and Affiliation:

Sonia Maqbool[1], Mohsin Raza[2]
[1-]Sheikh Zayed Hospital Rahim Yar Khan, Pakistan,
[2]Nishtar Hospital, Multan , Pakistan.
[*]**Corresponding Author Email**: soniamaqbool635@gmail.com

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Original Article

Comparison of Calcium Carbonate versus calcium acetate in Chronic Kidney Disease (CKD) 5 patients

Sonia Maqbool[1], Mohsin Raza[2]
[1-]Sheikh Zayed Hospital Rahim Yar Khan, Pakistan,
[2]Nishtar Hospital, Multan , Pakistan.
[*]**Corresponding Author Email**: soniamaqbool635@gmail.com

ABSTRACT

Objective*: To compare the phosphate binding power and hypercalcaemic effect of calcium acetate and calcium carbonate in chronic kidney disease stage 5 patients.*

Methods*: The study was conducted in the Department of Nephrology at Shaikh Zayed Complex/DHQ Hospital Rahim Yar Khan, after approval from The College of Physicians and Surgeons of Pakistan. Informed written consent was obtained from all participants after full disclosure. Patients were randomized into groups A and B using the lottery method. Group A received CaAc, while group B received $CaCo_3$. The study had four phases. In phase 1, both groups underwent a two-week washout, stopping phosphate binders. Baseline tests followed. In phase 2, group A received 4.002 g/day of CaAc (1.014 g elemental calcium), while group B took 5.625 g/day of $CaCo_3$ (2.25 g elemental calcium) for four weeks. Phase 3 ended with another two-week washout without phosphate binders.*

Results*: The mean serum urea of Group A and Group B was 27.44±2.19 mg/dl and 29.36±3.19 mg/dl, respectively. (p=0.008). The mean serum creatinine of Group A and Group B was 1046.11±120.95 mg/dl and 1104.76±116.52 mg/dl, respectively. The mean serum albumin of Group A and Group B was 39.32±4.78 g/l and 30.66±5.45 g/l, respectively. The mean final serum calcium level of Group A and Group B was 2.48±0.52 mmol/L and 2.53±0.18 mmol/L, respectively. The mean final serum PO4 level of Group A and Group B was 1.72±0.43 mmol/L and 1.82±0.50 mmol/L, respectively.*

Conclusion: *Patients undergoing maintenance hemodialysis experience comparable serum phosphate level reductions from calcium acetate and calcium carbonate treatments. Calcium acetate results in fewer cases of hypercalcemia while maintaining similar drug tolerance compared to calcium carbonate.*

Keywords*: Hyperphosphatemia, Calcium acetate, Chronic Kidney disease, Calcium carbonate*

1. INTRODUCTION

Chronic Kidney Disease (CKD) stands as an essential public health issue globally since it impacts about 13.4% of people around the world, which translates to roughly 843.6 million affected individuals. The occurrence of CKD in Pakistan displays a wide range from 12.5% to 29.9%, according to various research studies. Research findings show that 12.86 million Pakistanis above thirty years old suffer from renal impairment, which shows the significant disease burden Pakistan faces.

Patients with CKD stage 5 frequently develop hyperphosphatemia because their kidneys are unable to excrete phosphate properly. High serum phosphate concentrations cause secondary hyperparathyroidism together with vascular calcification, which results in higher rates of disease and death. Patient populations must manage hyperphosphatemia effectively to reduce associated risks.Physicians often prescribe calcium-based phosphate binders, calcium carbonate and calcium acetate, to manage serum phosphate levels in patients with CKD. The agents work within the gastrointestinal tract to connect with dietary phosphate and prevent absorption. The differences in efficacy and safety profiles between these binders require comparative analysis to establish the best therapeutic approaches.

Multiple investigations have assessed the performance of calcium acetate compared to calcium carbonate for treating hyperphosphatemia. The meta-analysis results demonstrate that calcium acetate performs equally well as calcium carbonate in reducing serum phosphate levels among chronic dialysis patients. Calcium acetate exhibits improved solubility under acidic and alkaline pH conditions, which may lead to a better phosphate-binding ability.

Even though study findings exist, calcium-based binders maintain issues related to hypercalcemia and gastrointestinal intolerance. Calcium acetate treatment shows a higher incidence of hypercalcemia episodes. A thorough evaluation of calcium carbonate versus calcium acetate is crucial for assessing their effectiveness and safety in treating hyperphosphatemia in CKD stage 5 patients.

2. METHODOLOGY

Study was conducted at Department of Nephrology at Shaikh Zayed Complex/DHQ Hospital Rahim Yar Khan, after permission from The College of Physicians and Surgeons of Pakistan, and we obtained informed written consent from all study participants following thorough information disclosure about the research. The lottery method was used to randomize patients into A and B groups. The researchers administered CaAc to group A and gave group B CaCo3 for treatment. The study was conducted in four phases. During phase 1, both groups entered a two-week washout period, during which they stopped using phosphate binders. Baseline tests were performed following this period. Group A began receiving 4.002 g/day of CaAc containing 1.014 g elemental calcium in phase 2, while group B started on 5.625 g/day of CaCo3 with 2.25 g elemental calcium for four weeks. No phosphate binders were administered during the two-week washout following phase 3. The crossover design in phase 4 resulted in group A receiving CaCo3, while group B received CaAc for an additional four weeks. The study required patients to consume their prescribed medications during meals. Throughout the study, researchers measured urea, creatinine, calcium, albumin, and phosphate serum

levels during each phase and documented the results using a predesigned proforma.

The participants for the study were patients suffering from Chronic Kidney Disease (CKD) 5 and were aged between 20 and 60 of both genders. Patients with CKD stage I to IV, those with previous parathyroidectomy, and advanced malignancy or sitting metastasis were excluded from the study. There was no systematic sampling; a non-probability technique was employed. Using an online sample size calculator, the sample size was set at 50 owing to the 95% confidence level and 80% study power. Previous results indicate those taking CaCo3 had serum calcium levels at 2.73 ± 0.67 mmol/L, while those on CaAc were at 2.32 ± 0.28 mmol/L. The sample was divided evenly into two groups, with 25 patients in each group.

This study sought to assess the effectiveness of calcium acetate (CaAc) versus calcium carbonate (CaCo3) in patients with chronic kidney disease stage 5 (CKD 5), with an estimated glomerular filtration rate (72) eGFR < 15 mL/min/1.73 m^2 for greater than three months and not on kidney replacement therapy. Effectiveness was evaluated in terms of phosphate-binding power as well as hypercalcemic impact. Bound power was defined as the capacity to keep serum phosphate at a normal level between 3.4 and 4.5 mg/dL. In comparison, a hypercalcemic effect was characterised by increased serum calcium levels over the standard mark of 10 mg/dL. It was believed that calcium acetate would result in a lower incidence of hypercalcemia than calcium carbonate while having the same level of phosphate-binding power.

Analysis of the data was done using SPSS software version 24. Mean and standard deviation were established for the numerical variables of age, duration of dialysis, and level of CaAc, CaCo3, phosphate, and albumin. Proportional frequency and percentages were established for the categorical variables of sex and treatment groups. Possible confounding and effect-modifying factors such as age, sex, and duration of dialysis were controlled for by stratification. A post-stratification t-test was performed for numerical variables, while qualitative variables compared using chi square test with significant p-value of ≤ 0.05.

3. RESULTS

A total of 60 patients were included in our study, with 30 patients (50.0%) in Group A (CaAc) and 30 patients (50.0%) in Group B (CaCo2). The mean age of patients in Group CaAc was 42.10±6.87 years, while in Group CaCo2, it was 41.03±5.77 years (p=0.518). In Group CaAc, there were 19 males (63.3%) and 11 females (36.7%), whereas Group B had 21 males (70.0%) and 9 females (30.0%). The mean duration of dialysis was 31.93±8.48 months in Group CaAcand 32.13±6.04 months in Group CaCo2, (p=0.917).

The mean serum calcium levels in Group CaAc and Group CaCo2 were 2.74±0.85 mmol/L and 2.73±0.46 mmol/L, respectively (p=0.985). The mean serum phosphate (PO_4) levels were 1.47±0.32 mg/dL in Group CaAc and 1.69±0.51 mg/dL in Group CaCo2, showing a borderline difference (p=0.051). The mean serum urea levels were significantly different, with GroupCaAc at 27.44±2.19 mg/dL and Group CaCo2 at 29.36±3.19 mg/dL (p=0.008). The mean serum creatinine levels were 1046.11±120.95 mg/dL in Group CaAc and 1104.76±116.52 mg/dL in Group CaCo2, (p=0.061). However, the mean serum albumin levels were significantly lower in Group CaCo2 (30.66±5.45 g/L) compared to Group CaAc (39.32±4.78 g/L).

At the final assessment, the mean serum calcium levels were 2.48±0.52 mmol/L in Group CaAc and 2.53±0.18 mmol/L in Group CaCo2 (p=0.642). Similarly, the mean final serum phosphate levels were 1.72±0.43 mmol/L in Group CaAc and 1.82±0.50 mmol/L in Group CaCo2, (p=0.408).

Table:I
Demographics profile of the study groups

Variable	Group A (CaAc)	Group B (CaCo3)	p-value
Age (years)	42.10±6.87	41.03±5.77	0.518
Gender			
Male	19 (63.3)	21 (70.0)	0.584
Female	11 (36.7)	9 (30.0)	
Duration of dialysis (months)	31.93±8.48	32.13±6.04	0.917
N (%)chi-square test was applied, Mean±S.D independent samples t test was applied.			

Table: II
Comparison of post- crossover stage of the study groups

Variable	Group A (CaAc)	Group B (CaCo3)	p-value
Serum Calcium (mmol/l)	2.74±0.85	2.73±0.46	0.985
Serum PO4 (mg/dl)	1.47±0.32	1.69±0.51	0.051
Serum urea (mg/dl)	27.44±2.19	29.36±3.19	0.008
Serum creatinine (mg/dl)	1046.11±120.95	1104.76±116.52	0.061
Serum albumin (g/l)	39.32±4.78	30.66±5.45	<0.001
Mean±S.D, independent samples t test was applied.			

Table: III
Comparison of outcomes of the study groups

outcome	Group A (CaAc)	Group B (CaCo3)	p-value
Final serum calcium level (mmol/L)	2.48±0.52	2.53±0.18	0.642
Final serum PO4 level (mmol/L)	1.72±0.43	1.82±0.50	0.408
Mean±S.D, independent samples t test was applied.			

4. DISCUSSION

Calcium acetate (CaAc) is generally considered to be better tolerated than calcium carbonate ($CaCO_3$), as it has a lower risk of causing gastrointestinal discomfort and other adverse effects. Additionally, calcium acetate exhibits superior phosphate-binding efficacy, particularly in patients with chronic kidney disease, as it binds dietary phosphate more effectively even at lower doses[11]. This enhanced phosphate-binding capacity helps in better management of hyperphosphatemia. Furthermore, calcium acetate is associated with a lower incidence of hypercalcemia compared to calcium carbonate, likely due to its improved solubility and bioavailability, which result in a more controlled release of calcium into the bloodstream, thereby reducing the likelihood of excessive serum calcium levels[12]

A statistically significant increase in calcium (Ca) levels was observed in patients while they were taking calcium carbonate ($CaCO_3$). However, international studies conducted by Ben et al[13] and Moniere et al[14] contradicted the notion that calcium acetate (CaAc) has a lesser hypercalcemic effect, suggesting that its impact on serum calcium levels may not be significantly different from that of calcium carbonate.

A prospective double-blind crossover comparison conducted by Ring et al[15] suggests a higher frequency of hypercalcemia with the use of calcium acetate (CaAc). However, certain differences in the study design may account for the observed discrepancies. These differences could include variations in patient selection criteria, dosing regimens, duration of treatment, or methods used to assess and monitor calcium levels. Additionally, differences in baseline characteristics of the study population or variations in concomitant

medications and dietary calcium intake might have influenced the outcomes.

Similarly, a study conducted by Saif et al[16] concluded that while both calcium acetate and calcium carbonate have a comparable effect in lowering serum phosphate levels, calcium carbonate has a higher propensity to cause hypercalcemia than calcium acetate. Additionally, research conducted by Naghibi et al[17] on the Iranian population reported that calcium acetate is a more effective phosphate binder than calcium carbonate, further supporting its potential advantages in managing hyperphosphatemia.

A study conducted by Phelps et al[18] reported that serum phosphate levels were lower following treatment with calcium acetate compared to calcium carbonate. Additionally, the calcium-phosphorus (Ca × P) product and parathyroid hormone (PTH) levels were significantly reduced after treatment with calcium acetate, indicating its potential benefits in managing mineral metabolism. Similarly, research conducted by Wang et al[19] suggested that calcium acetate is more effective in controlling hyperphosphatemia than calcium carbonate, further supporting its clinical utility in patients requiring phosphate regulation.

Calcium acetate is highly soluble in both acidic and alkaline pH, making it an effective phosphate binder. It contains about 25% elemental calcium, whereas calcium carbonate has 40%. This means one gram of calcium acetate provides more available calcium than calcium carbonate[20].

5. CONCLUSION

Patients undergoing maintenance hemodialysis experience comparable serum phosphate level reductions from calcium acetate and calcium carbonate treatments. Calcium acetate results in fewer cases of hypercalcemia while maintaining similar drug tolerance compared to calcium carbonate.

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